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EXAMINER

TON, THAIAN N

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 05/29/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/654,293	CHRSTMANN ET AL.
	Examiner Thai-An N. Ton	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 17 March 2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-6, 14-22, 24-26, 28, 30, 32 and 33 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-6, 14-22, 24-26, 28, 30, 32 and 33 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____.
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) II 6) Other:

DETAILED ACTION

Applicants' Amendment, filed 3/17/02, Paper No. 13, has been entered. Claims 1, 14, 19-21, 24-26, 28, 30 have been amended. Claims 11, 27, 29 and 31 have been cancelled.

Claims 1-6, 14-22, 24-26, 28, 30, 32 and 33 are pending and under current examination.

Any rejection made of record in the prior Office action, mailed 9/12/02, Paper No. 10, and not made of record in the instant Office action, has been withdrawn in view of Applicants' arguments and/or amendments to the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 1-6, 14-22, 24-26, 28, 30, 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is *maintained* for reasons of record advanced on pages 2-7 of the prior Office action.

The claimed invention is directed to cloned chickens, methods of producing cloned chickens, methods of producing reconstructed chicken zygotes or oocytes, and methods of producing a protein from the cloned chickens.

Applicants' arguments and amendments to the claims have been carefully considered; however, they are not found persuasive. Applicants argue that, with regard to the Examiner's assertion that the specification fails to provide sufficient guidance or teachings to show that cloned avian can be made by the methods described is not applicable to the claims as amended. Rather, the claims as amended refer to chickens rather than avian. Applicants point to the specification to provide support in the specification wherein the claimed method is illustrated in chickens. See pp. 8-9 of the Response.

Applicants argue that the specific working examples [pp. 31-36 of the specification] presented in the specification enable the claimed method. For example, Applicants state that they have shown that the ova were isolated from euthanized hens, or from eggs isolated from hens with fistulated oviducts; dye was then injected into the germinal disk of the ovum; images of the inside of the avian early embryo were obtained through the use of two photon laser scanning microscopy [TPLSM] by placing the germinal disk on the microscope and searching for the pronuclear structures within the central area of the disk; once found, the nuclear structures were ablated by laser mediated ablation, a donor nucleus was then isolate, and a reconstructed zygote was prepared via localization and

positioning of the germinal disk under the microscope and subsequently guided injection of the somatic cells. Applicants state that the donor ovum is then placed into the recipient hen through a surgical procedure, wherein the ovum is allowed to move into the infundibulum and into the interior magnum by gravity feed. The recovery time for the bird is 45 minutes, the eggs are subsequently laid by the recipient hen and collected and incubated and chicks hatch 21 days later. Applicants contend that in light of the amendment, the claims are in condition for allowance. See pp. 8-9, bridging ¶.

Applicants' arguments are not found to be persuasive. In particular, it is maintained that the specification fails to provide guidance or teachings to show that cloned chicken could be produced the claimed method of nuclear transfer. It is noted that the specification teaches general methods of ovum transfer; however, it does not provide specific teachings with regard to the generation of a cloned chicken. See Example 4, pages 35-36 of the specification.

MPEP §2164.03 states that:

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability.

The Examiner maintains that the nuclear transfer art is unpredictable. The prior Office actions have provided support for this by providing art which points to the numerous unpredictable factors which affect the cloning of animals, and the unpredictability in the state of the art of nuclear transfer, which is such that one of skill in the art could not predictably produce cloned or transgenic chickens without specific teachings provided by the specification [see pp. 6-7 of Office action mailed 12/5/01, Paper No. 6].

The claimed invention is directed to methods of producing cloned chicken zygotes [claims 1-6], cloned chickens [claims 14-18, 30] and methods of producing transgenic chickens [claims 19-21]. These claims are not enabling because they fail to provide a step of transferring the resulting NT unit to a recipient hen of the same species. The only guidance provided by the specification is by transferring a reconstructed zygote or embryo to the oviduct of a recipient hen to produce a hard shell egg, which can then be incubated to generate a cloned chick. See p. 22, lines 5-14, of the specification. The claims, as written, are not enabling because they merely recite that the reconstructed zygote/oocyte are allowed to develop to term. Clearly, merely culturing the reconstructed zygote/oocyte will not produce a hard shell egg, which could then be incubated to produce a live chick.

Applicants argue that the amended claims now indicate that the claimed methods are used "for generation of a transgenic chicken" which overcomes the prior rejection that the specification fails to provide specific teachings or guidance

as to how to use the claimed reconstructed avian zygotes or oocytes. See p. 10, 1st full ¶.

Applicants' arguments have been considered, however, they are not found to be persuasive. In particular, the Examiner's prior rejection is with regard to the fact that although the specification provides guidance for the production of a reconstructed chicken zygote or oocyte, the specification fails to provide an enabled use for the chicken zygote or oocyte. For reasons stated *supra*, the generation of transgenic chickens and cloned chickens is not predictable. As the specification *only* teaches this use for the reconstructed chicken zygote or oocyte, the specification fails to teach an enabled use for the claimed zygotes or oocytes.

Additionally, in the prior Office actions, the Examiner has provided references with regard to the unpredictability in the state of the art of transgenesis [see pp. 6-7 of the Office action mailed 12/15/01, Paper No. 6]. As such, it is reiterated that the expression of the transgene and the effect of transgene expression on the phenotype of the transgenic animal depends on the particular gene construct used, to an unpredictable extent. With the lack of working examples provided by the specification, as well as the unpredictability in the art, one of ordinary skill in the art would have been required to engage in undue experimentation in order to make and use the claimed transgenic chicken.

Therefore, in view of the quantity of experimentation necessary to determine the parameters for nuclear transfer for the production of reconstructed chicken

zygotes, oocytes or cloned or transgenic chickens, the lack of direction or working examples provided by the specification for the production of cloned or transgenic chickens, as well as the unpredictable state of the art of nuclear transfer and transgenics, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, as written, is incomplete. The claim recites that the reconstructed zygote or oocyte is allowed to develop to term. See part (vi) of the claim. This is incomplete because development of a chicken zygote would require such steps as transfer to a recipient hen of the same species, the laying of a hard-shell egg, and further incubation, for example, to produce a chicken. Claims 2-6, 28, 30 depend from claim 1.

Claims 14 and 19, as written, are incomplete. The claims recite that the reconstructed zygote or oocyte is allowed to develop to term. See part (vii) of the claim. This is incomplete because development of a chicken zygote would require such steps as transfer to a recipient hen of the same species, and laying of an egg, and further incubation, for example, to produce a chicken. Claims 15-18, 24 depend from claim 14. Claims 20, 21, 25 depend from claim 19.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 25 is rejected under 35 U.S.C. 102(a) as being anticipated by WO 00/11151, [Ivarie *et al.*] published 2 March 2000, Citation AA, on IDS filed 9/30/02.

The claim is directed to an intact hard shell egg produced by the method of claim 21 containing exogenous protein. Note that the claim is a product by process claim. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, *supra*. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685. (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process,

determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.”

As such, the claim is properly interpreted as an intact hard shell egg containing exogenous protein. Ivarie teach that white Leghorn pullets were injected in two or three locations into the lumen of the magnum of the oviduct with 0.5-0.6 ml of particles [VSV-G typed NLB-CMV-IFN-MM]. Twelve weeks later, eggs were collected from laying hens and assayed for the presence of interferon in the egg white. See Example 4, pages 37-39.

Accordingly, Ivarie teach the claimed invention.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/19472 [Ivarie *et al.*], published 22 April 1999, Document B8, in IDS filed 3/21/01.

The claim is directed to an intact hard shell egg produced by the method of claim 21 containing exogenous protein. Note that the claim is a product-by-process claim. See *supra*. As such, the claim is properly interpreted as an intact hard shell egg containing exogenous protein. Ivarie teach that stage X chicken embryos in freshly laid eggs were transduced with NLB-CMV-BL transduction particles [encoding beta-lactamase]. Chimeric founder hens began to lay eggs and the egg whites were assayed for the presence of β-lactamase, and it was found significant

levels were detected in the egg white of six hens [see Figure 4, Table 1 and Example 3].

Accordingly, Ivarie teach the claimed invention.

The prior rejection of claim 26 under 35 U.S.C. 102(b) as being anticipated by Chang *et al.* [*Cell Biology International*, 21:495-499, 1997] is *maintained* for reasons of record.

Claim 26 is directed to a reconstituted avian embryo prepared by transferring the nucleus of a donor cell into a suitable recipient cell.

Applicants claim that a “reconstructed embryo” is a term that has meaning in the art; that the art understands the definition of a reconstructed embryo to mean an embryo that results from the transfer of a donor nucleus into a cytoplasm. Thus, Applicants conclude that that a reconstructed embryo means an embryo wherein the nucleus of a donor adult cell is inserted into an enucleated egg; and thus, the cited art does not teach the claimed invention.

Applicants’ arguments have been considered, but they are not found to be persuasive. The Examiner agrees with Applicants’ arguments that a reconstructed embryo is an embryo that is made by a method of nuclear transfer. However, Applicants are claiming the resulting embryo. The embryo, as taught by Chang *et al.* anticipates the claimed invention because they teach an embryo. The patentability of a product does not depend upon its method of production. A chicken

embryo, as taught by Chang *et al.* would be considered identical to a chicken embryo produced by NT method.

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, *supra*. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

As such, the claim is properly interpreted as a chicken embryo. Chang *et al.* teach the injection of cultured PGCs into recipient embryos obtained from the Korean native ogol chicken [see p. 496, 1st column].

Accordingly, Chang *et al.* anticipate the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tháí-An N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to William Phillips, Patent Analyst, at (703) 305-3482. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

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